

REMARKS

Claims 1-26 are pending. Applicants have cancelled claims 1-11 and 13-25, amended claims 12 and 26 as follows, and added claims 27-28. Applicants make these amendments in order to expedite prosecution of these claims. Support for these amendments appears throughout the specification and claims as originally filed. Claims 12 and 26 are supported at page 3, lines 6-10, original claims 12 and 26, and Example 9 in the specification as filed. Claims 27 and 28 are supported by original claims 14 and 15. No new matter is added by these amendments. Applicants make such amendments without prejudice to pursuing the originally presented or cancelled subject matter in a later application claiming benefit of this application, and particularly without prejudice to determination of equivalents of subject matter of this application or any later application claiming benefit of this application.

Rejection under 35 U.S.C. §102(b)

Claims 1-12 are rejected as anticipated by Schutt (U.S. Patent 4,248,861). It is alleged that Schutt teaches a skin composition comprising kava kava, and that kava kava contains all the kavalactones claimed in Applicants' claims.

The Schutt compositions contain 0.5 to 3 parts kava kava extract. Kava kava extract includes a number of various kavalactones, i.e. more than sixteen. Of these, kawain, dihydrokawain, and dihydromethysticin make up about 40% - 60% of the total kavalactone content. Thus, Schutt describes compositions having about 0.006% – 0.4% total content of those three kavalactones. Such compositions are distinguishable from Applicants' compositions.

Applicants have discovered that the combination of kawain, dihydrokawain, and dihydromethysticin provides superior inhibition of IL-12 relative to other kavalactones. See, Specification at page 4, lines 22-23 and Figure 1. Applicants have amended claims 12 and 26 to recite compositions having 5% to 25% by weight active kavalactones that are the combination of kawain, dihydrokawain, and dihydromethysticin. As such, Schutt does not anticipate

Applicants' claimed subject matter as amended, and Applicants respectfully request withdrawal of this rejection.

It is further alleged that Claims 1-12 are anticipated by Rosenbaum (U.S. Patent 5,585,386). It is alleged that Rosenbaum teaches a topical composition comprising kavain, dihydrokavain, methysticin, dihydromethysticin and a physiologically acceptable carrier. Applicants disagree. Rosenbaum exemplifies compositions having either kavain or methysticin, but does not exemplify compositions having dihydrokavain, dihydromethysticin, nor any combination of any kavalactones.

The Rosenbaum compositions have at least one  $\alpha$ -pyrone compound of a structural formula that describes three variable positions, each having one of five, two, and 24, possible substituents at their respective positions. Rosenbaum, however, does not describe any combinations of kavalactones, nor even discusses a preference for any two kavalactones. Rosenbaum states a preference for the kawain, and 5-methylvalerolactone, which is not a kavalactone. As Rosenbaum does not disclose combinations of two kavalactones, nor two or more kavalactones, nor the specific combination of kawain, dihydrokawain, and dihydromethysticin as claimed by Applicants, Applicants submit that Rosenbaum does not anticipate Applicants' claimed subject matter (as amended) and request that this rejection be withdrawn.

Claims 1-12 are rejected as anticipated by Kubo (Japanese Patent 11-189541). It is alleged that Kubo teaches a topical skin lotion or ointment comprising extracts of *Piper Methysticum*. It is then concluded that the Kubo compositions anticipate Applicants' claims 1-12. Applicants disagree for reasons stated above for Schutt.

The Kubo compositions contain 0.0001% to 20% parts kava kava root extract. Kava kava extract includes a number of various kavalactones, i.e. more than sixteen. Of these, kawain, dihydrokawain, and dihydromethysticin make up about 40% - 60% of the total kavalactone content. Thus, Kubo describes compositions having 0.00012% - 2.4% total content of the three kavalactones.

Applicants have amended claims 12 and 26 to recite compositions having 5% to 25% by weight active kavalactones that are the combination of kawain, dihydrokawain, and

dihydromethysticin. As such, Kubo does not anticipate Applicants' claimed subject matter as amended, and Applicants respectfully request withdrawal of this rejection.

Rejection under 35 U.S.C. §103(a)

Claims 1-12 are rejected as obvious in light of any of Schutt, Rosenbaum or Kubo. In each instance, it is alleged that while the reference does not expressly teach the entire concentration range for kavalactones, one of ordinary skill in the art would be motivated to do this to provide different dosage levels for different skin types or to adjust concentration according to different ingredients being included in the composition. Applicants disagree with this assertion.

Applicants have identified a combination of three particular kavalactones: kawain, dihydrokawain, and dihydromethysticin that provides therapeutic effect for IL-12 modulation. See, Specification at page 4, lines 22-23, and Figure 1. This superior inhibitory effect of the combination of kawain, dihydrokawain, and dihydromethysticin was not heretofore recognized. The rejection is based on the impermissible use of hindsight upon reading Applicants' disclosure. Neither Schutt, Rosenbaum, nor Kubo provide any motivation to one of ordinary skill at the time of the invention to select the particular combination of kavalactones (i.e., kawain, dihydrokawain, and dihydromethysticin), let alone any particular range of the combination of those three kavalactones.

Schutt and Kubo describe compositions based on kava kava extract. As stated above, the compositions of Schutt and Kubo include kava kava extract, which includes a variety of kavalactones in their respective indicated proportions. These compositions are distinguishable from Applicants' compositions having kawain, dihydrokawain, and dihydromethysticin in a range of between 5% and 25%, by weight. Neither Schutt nor Kubo provide any guidance to one of ordinary skill at the time of the invention to arrive at the combination of three specific kavalactones in the claimed proportions. For that matter, neither Schutt nor Kubo even provide guidance to the desirability of any particular combination of kavalactones.

The Rosenbaum compositions have at least one  $\alpha$ -pyrone compound of a structural formula that describes three variable positions, each having one of five, two, and 24, possible

substituents at their respective positions. Thus, a plethora of possible compounds are encompassed by this description. The source of these  $\alpha$ -pyrone compounds varies as well. For example, the  $\alpha$ -pyrone compounds are found in piper methysticum (kava kava), Sorbus aucuparia berries, and Avena Sativa. Thus, these  $\alpha$ -pyrone compounds described by Rosenbaum represent a number of compounds that are not kavalactones (i.e., compounds derived from kava kava). Further, Rosenbaum teaches (including for example in claims 2-12) compositions wherein the  $\alpha$ -pyrone is one of 11 different  $\alpha$ -pyrone. Rosenbaum also discloses one combination of two  $\alpha$ -pyrone compounds, and in fact refers to it as "preferred" (see col. 3, lines 17-18); however, that combination is of a kavalactone (kavain) and a compound derived from Avena Satina (5-methylvalerolactone), which is not a kavalactone. Thus, Rosenbaum does not disclose any particular combination of two kavalactones, nor for that matter any combination of more than two kavalactones. Moreover, the examples in Rosenbaum (i.e., Examples 1, 3, and 4) only contain a single kavalactone. (i.e., kavain or methysticin).

There is no guidance in any of those three cited references to direct one of ordinary skill to Applicants' claimed subject matter, that is, compositions having between 5% and 25% of a combination of kavain, dihydrokavain, and dihydromethysticin; a combination having surprising and superior inhibitory activity against IL-12. As such, one of ordinary skill at the time of the invention would not be motivated to arrive at Applicants' claimed subject matter with a reasonable expectation of success.

Claims 13-20 are rejected as obvious in light of Asmussen (U.S. Patent 6,379,696) in view of Elbakyan (WO 00/30578) and further in view of Schwabe (U.S. Patent 5, 296,224). In the Action, it is alleged that Asmussen teaches a transdermal therapeutic system comprising kavain, that Elbakyan teaches a transdermal patch system comprising an active agent, and that Schwabe teaches that kavain is a kavalactone. It is then concluded that it would have been obvious to one of ordinary skill to provide a slow release therapeutic composition. Applicants disagree.

One of ordinary skill would not have been motivated by any of Asmussen, Elbakyan, or Schwabe to arrive at Applicants' claimed subject matter, a transdermal patch having a combination of kavain, dihydrokavain, and dihydromethysticin in a range between about 5% and 25%. Asmussen, Elbakyan and Schwabe do not, either alone or in combination, disclose the

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specific combination of three kavalactones (i.e., kawain, dihydrokawain, and dihydromethysticin), or the specific range by weight of those three components as Applicants have. As such, no evidence is cited in the Action that would have motivated one of ordinary skill to arrive at Applicants' claimed subject matter (as Amended) at the time of invention.

Attached is a marked-up version of the changes being made by the current amendment. Applicants ask that all claims be allowed. Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 13321-003001.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 1-11 and 13-25 have been cancelled.

Claims 12 and 26 has been amended as follows:

12. (Amended) [The medicinal ointment of claim 9] A medicinal ointment comprising 5% to 25% by weight an active kavalactone, wherein the active kavalactone is a combination of dihydromethysticin, dihydrokawain, and kawain.

26. (Amended) [The patch of claim 23] A patch comprising a material layer and a composition associated with the material layer; the composition having 5% to 25% by weight an active kavalactone, wherein the active kavalactone is a combination of dihydromethysticin, dihydrokawain, and kawain.